OL. XI, No. 1 JANUARY, 1950

610.5
B73

MAR 30 1950

BORDEN'S REVIEW

of

NUTRITION RESEARCH

NUTRITION HIGHLIGHTS — 1949

BORDEN'S REVIEW
of
NUTRITION RESEARCH

Reviews and summaries of research information concerning nutrition and foods. Published monthly, except July and August, by THE BORDEN COMPANY; officers of the Company: Theodore G. Montague, president; E. L. Noetzel, treasurer; T. D. Waibel, secretary. Editorial office: 350 Madison Avenue, New York 17, N. Y.

NUTRITION HIGHLIGHTS — 1949

By RUTH WOODS

The year 1949 has been both a busy and fruitful one with respect to achievements in nutrition. These achievements have contributed liberally not only to an understanding of basic concepts in nutrition and biochemistry, but to a more extensive application of the fundamental principles of nutrition to practical problems in human health and disease. More and more, theoretical findings with the rat, guinea pig and bacteria—to cite a few of the many forms of animal life contributing to modern scientific knowledge —have been translated in terms of their significance in human welfare.

The record of nutrition progress during 1949 has included several important discoveries: The protein requirement for the adult human in terms of amino acids needed to maintain nitrogen balance; further delineation of the biological function and mutual interrelationship of the vitamins, minerals and amino acids; possible existence of several new vitamin factors; the increasing use of radioisotopes to detect the course of metabolism of basic food components; increased insight into the role of foods in the maintenance of tissue integrity and general health.

The present paper, by no means a comprehensive survey of the many outstanding activities during 1949, will describe briefly a few, representative studies which may be of particular interest to the readers of *Borden's Review of Nutrition Research.*

Amino Acid Requirements of Man:

In April, 1949 quantitative values for the amino acids essential in human nutrition were reported for the first time by Rose terminating many years of intensive research on the general significance of amino acids in nutrition. With the isolation and identification in 1936 of the new amino acid, threonine, it became possible for the first time to support animal growth on diets containing mixtures of highly purified amino acids in place of proteins. By the successive removal from such diets of single amino acids, the nutritive role of each was established. By this means, ten of the 20-odd amino acids were shown to be essential for the growing rat: valine, leucine, isoleucine, threonine, methionine, phenylalanine, tryptophane, lysine, histidine and arginine. Exclusion of any one of these, except arginine, leads to severe nutritive failure — loss of appetite, loss in weight, death. Arginine deficiency merely decreases the rate of weight gain, indicating that unlike the other

nine it can be synthesized by the rat, but not at a sufficiently rapid rate to meet the needs for maximum growth.

Beginning in 1942, comparable studies were begun with healthy adult human subjects, the list of essential amino acids being completed by 1947. The amino acids required by adult man for the maintenance of nitrogen balance were found to be identical with those previously found essential for maximum growth in the rat, with the exception of arginine and histidine. Whether, as in the rat, these are not required for adult maintenance, but may be necessary for efficiency of growth in the child remains to be determined. Having established qualitatively the amino acid requirements of normal man, *quantitative* studies were next undertaken. The object was to discover the minimum intake of each of the eight essentials which is capable of permitting nitrogen balance when the diet furnished sufficient amounts of the other seven and an adequate supply of nitrogen for the synthesis of the non-essential amino acids. These studies have culminated in the following results:

Minimum and Recommended Intakes for Normal Man when Diet Furnishes Sufficient Nitrogen for Synthesis of Non-Essential Amino Acids.
(Strictly Tentative Values)

Amino Acid	Minimum Daily Rqt. (gm.)	Recommended Daily Intake (gm.)
L-Tryptophane	0.25	0.5
L-Phenylalanine	1.10	2.2
L-Lysine	0.80	1.6
L-Threonine	0.50	1.0
L-Valine	0.80	1.6
L-Methionine	1.10	2.2
L-Leucine	1.10	2.2
L-Isoleucine	0.70	1.4

—*Fed. Proc. 8*, 546 (1949) —*J. Biol. Chem. 181*, 307 (1949)

Growth Factor In Milk:

The intestinal microorganism, *Lactobacillus bifidus,* is found in predominant numbers in infants receiving only human milk. Because of the possible importance of this microorganism to infant health, studies of its nature and nutritional requirements have been undertaken. It has been found that the growth of *L. bifidus* mutants isolated from the stools of breast-fed infants is dependent upon the presence in a semisynthetic medium of an unsaturated fatty acid factor provided by supplements of either human or cow's milk.

Concentration of the factor was five times as great in human milk. Digested human and cow's milk exhibited superior growth activity, but indications of an antagonistic growth inhibitor were also found. Too high concentrations of cow's milk permitted the inhibitor to function; in human milk the effect of the inhibitor was nullified by the abundance of growth factor. *L. bifidus* mutants also exhibited a need for an unidentified stimulatory factor present in enzymatic digests of casein, pancreatin, or trypsin preparations. Desoxyribosides (such as thymidine), but not vitamin B_{12}, were found to exert activity similar to that of the enzymatic factor.

—*J. Biol. Chem. 181,* 879 (1949)

Vitamin B_{12}*:*

Vitamin B_{12}, the anti-pernicious anemia factor of liver, was isolated and purified last year after more than twenty-two years of intensive research by numerous investigators. During 1949 vitamin B_{12} has been found to be of vital importance in a multitude of biological reactions other than those involved in blood regeneration. Hailed as the "nutritional find of the year" it is already commercially available as an essential growth supplement to grain rations in poultry and hog feeds. Partial identification of its chemical structure has been announced* and many significant interrelations have been established between this vitamin and other nutritional factors. It is now known to be intimately involved with folic acid, ascorbic acid and the lipotropic factors (choline, methionine and betaine). It functions not only as an anti-anemia compound, but plays an important role in transmethylation, in child growth and in appetite stimulation; in counteracting thyrotoxic agents; and in protecting against liver injury, to cite a few of its many activities.

Vitamin B_{12}, Folic Acid and Vitamin C: Vitamin C has long been known to have an important function in blood-building processes and a deficiency of this vitamin is common in certain types of anemia. Evidence has now accumulated to indicate a direct interplay between vitamin C and the newer hematopietic factors, vitamin B_{12} and folic acid. The interrelations between B_{12} and folic acid have been described in detail.* Vitamin C and folic acid have been shown to share a common function in the intermediate metabolism of tyrosine.** The addition of vitamin C to a purified chick ration containing crude folic acid concentrates stimulates growth, as do also synthetic folic acid and vitamin B_{12}. Recent studies indicate a direct correlation between the level of folic acid stored in the liver and the rate of growth obtained. Addition of

---

**cf. Borden's Review of Nutrition Research,* "Recent Advances in the Knowledge of Anti-Anemia Factors," Nov. 1949.

***Borden's Review of Nutrition Research,* "Dietary Interrelationships — Vitamin C and the Metabolism of Aromatic Amino Acids," Sept. 1949.

either B_{12} or vitamin C, with or without folic acid, causes some increase of liver folic acid. Vitamin B_{12} and vitamin C, administered together, raise the liver storage level of folic acid appreciably—except when large amounts of folic acid are already present in the diet. The conclusion is reached that B_{12} and ascorbic acid act to stimulate the synthesis of folic acid. Other observations lead to the opinion that, conversely, folic acid stimulates the synthesis of vitamin B_{12}. Vitamin C however apparently does not spare this activity. The action of B_{12} and particularly of vitamin C in stimulating folic acid synthesis has been attributed to an oxidation-reduction mechanism which favorably affects vitamin synthesis by intestinal microflora.

—*J. Biol. Chem. 178,* 861 (1949) —*J. Biol. Chem. 181,* 915 (1949)

Animal Protein Factor and Transmethylation: A series of experiments with chicks has revealed an interesting interrelationship between methylating agents such as betaine and choline, and the animal protein factor (APF) of liver. A diet complete in all known vitamins and minerals except APF was significantly improved by additions of betaine or choline (0.2% of either betaine-HCl or choline-HCl). The addition of 0.15% liver extract paste in place of either of these, however, was even more effective. When this amount of liver paste was furnished, extra choline or betaine caused no further improvement. The choline content of the liver was found to be negligible (0.0018%). Its vitamin B_{12} activity was found to be about 17 micrograms per gram. Whether the activity of the liver in these studies was due to its B_{12} content or some other fraction of the animal protein factor complex* is not yet known. Nevertheless, it has been demonstrated that the inclusion of a source of APF in the diet relieves the need for supplementary methylating compounds under certain conditions. This is interpreted to indicate that at least one metabolic function of APF is concerned with methylation or with the synthesis of methyl groups. It appears probable either (a) that transmethylation is more efficient in the presence of an adequate amount of APF or (b) that a partial deficiency of APF creates or stimulates metabolic processes which require excess methyl groups. Studies by other investigators with crystalline B_{12} and B_{12} concentrates appear to support the theory that the active APF fraction contains vitamin B_{12}. The choline requirement of chicks receiving B_{12} was markedly reduced and, conversely, choline was found to have a significant sparing action on vitamin B_{12}. These investigators found, further, a protective action of vitamin B_{12} on the hemorrhagic kidney disease in rats on a low choline diet. Thirty mcgm. of the vitamin replaced

*cf. *Borden's Review of Nutrition Research,* "Recent Advances in the Knowledge of Anti-Anemia Factors," Nov. 1949.

about one-half of the choline or methionine needed to protect against kidney damage. Because of these interrelationships it is suggested that choline and methionine be tried clinically, as supplements to B_{12}, in the treatment of various types of human anemia.

—*J. Biol. Chem. 179,* 487 (1949)
—*J. Biol. Chem. 180,* 647 (1949)*
—*J. Biol. Chem. 181,* 109 (1949)
—*Proc. Soc. Exp. Biol. Med. 71,* 202 (1949)
—*Proc. Soc. Exp. Biol. Med. 71,* 193 (1949)

Vitamin B_{12} and Liver Injury: Vitamin B_{12} has been found to protect rats from the severe liver injury resulting from poisoning with carbon tetrachloride. The effect of the vitamin is not believed to be one which is related to the lipotropic action of choline or methionine since the animals were on a well-balanced diet presumably adequate in these factors. The mechanism involved is believed to be related to an effect of vitamin B_{12} on ribonucleic acid compounds* which are known to disappear early in liver injury.

—*Proc. Soc. Exp. Biol. Med. 71,* 688 (1949)

Vitamin B_{12} and Growth In Children: Daily oral doses of 10 mcgm. of crystalline B_{12} were given in addition to routine therapeutic measures to a group of eleven children suffering from growth failure and varying degrees of malnutrition. Dramatic improvements were noted in vigor, alertness and general behavior as well as in resumption of normal rates of progress in growth. A marked increase in appetite was manifested by demands for "second helpings" as contrasted with comparatively indolent food habits before. An unusual finding is described by the authors:

> "The most dramatic general effects were shown by Case 2, a boy with severe allergic bronchitis, whose sleep for 12 months before had been regularly interrupted by asthmatic attacks and whose daytime wheezing permitted little desire for food, not to mention time for eating it. His growth response was accompanied by a remarkable attenuation of symptoms; in fact these simply vanished during the first week, to the surprise of every attendant, lay or professional. What possible connections there may be between B_{12}, its influence on protein metabolism, and allergic disturbance, are questions for further investigation."

The authors conclude that these experiences indicate a syndrome which may be described as a B_{12} functional deficiency and that the condition is definitely benefited by oral therapy with the vitamin. As a final measure of effects they note that the growth responses were equivalent to another 100 to 240 days of regular institutional care without the help of vitamin B_{12}.

—*Science 110,* 651 (1949)

**cf. Borden's Review of Nutrition Research,* "Recent Advances in the Knowledge of Anti-Anemia Factors," Nov. 1949.

Vitamin B_{14}:

Evidence for the existence of a new anti-anemia factor, designated vitamin B_{14}, has been found. Studies with this new factor have led to some revisions in the concept of anti-anemia mechanisms. According to the investigators in this field, the anti-pernicious anemia factor is not formed by the interaction of the so-called "intrinsic" and "extrinsic" factors, but is a single factor—probably the new B_{14} or a closely related compound. The so-called "intrinsic" factor is believed to be one or more compounds—possibly folic acid, xanthopterin or derivatives—which do not combine with B_{14} to form a new anti-anemia principle, but merely act to facilitate the absorption of B_{14} or related materials. Further studies are underway to determine this.

—*Science 109,* 34 (1949)

Niacin Requirement:

The requirement for niacin has been shown to be markedly altered by the intake of other dietary components, particularly the amino acids and, according to very recent studies, by the nature of the dietary carbohydrate. Amino acid imbalances in certain proteins—notably those of corn and gelatin—have been found to heighten the requirement for niacin.* The essential amino acid, tryptophane, appears to be a precursor of the vitamin* for both experimental animals and man, and when present in sufficient amounts, reduces the need for dietary niacin. This explains in part the long-recognized strong anti-pellagra value of milk which is very low in niacin. It explains also the pellagragenic action of excess corn as being caused by (1) a deficiency of tryptophane as a source of niacin and (2) an imbalance of amino acids leading to an impairment in the transformation, tryptophane → niacin, in a diet which is already poor in niacin. Other studies now indicate a demonstrable difference in niacin requirement in the presence of various carbohydrates. The need for the vitamin is greater in the presence of fructose and sucrose and less on diets containing dextrin or starch than on a diet containing glucose. The reason for the increased need for niacin when fructose replaces glucose is not clear. The two sugars follow similar enzymatic pathways in the body, but it is known that they are handled differently in certain respects. To cite a few examples: intestinal absorption is different; their effects on blood lactic acid and respiratory quotient are different; fat deposition is less when fructose is fed instead of glucose. Which of these, or others, is responsible for the altered niacin requirement is not yet known.

—*J. Biol. Chem. 177,* 163 (1949) —*J. Biol. Chem. 181,* 1 (1949)

—*J. Biol. Chem. 177,* 461 (1949)

**cf. Borden's Review of Nutrition Research,* "Dietary Interrelationships: Nicotinic Acid-Trytophane," Dec. 1948.

Vitamin C and Cortical Hormones:

The high concentration of vitamin C in the adrenal gland is of considerable biological interest. Its relation to Addison's disease, abnormal pigmentation, albinism, and the metabolism of the melanin pigments, their various precursors and derivatives has been described recently.* Latest studies interrelating vitamin C with adrenal cortex activity indicate a marked influence of this vitamin on the anti-arthritic activity of the adrenal hormone, deoxycortone, (desoxycorticosterone). Deoxycortone, normally believed to have an action antagonistic to that of cortisone (another adrenal hormone, 17-hydroxy-11-dehydrocorticosterone, the anti-arthritic compound E) has been found to exert cortisone-like activity when administered in conjunction with vitamin C. The vitamin is given via injection in 1 mg. doses, five minutes after the deoxycortone. Relief of arthritic symptoms begins in 5 minutes; reaches a maximum in 15-30 minutes and persists for 2-6 hours. Repeated treatments have longer effects. No explanation for the mechanism of this action has been found as yet. If these findings are confirmed, the discovery will be a great step forward; for deoxycortone is manufactured synthetically and is relatively plentiful, whereas cortisone is extremely rare and is expected to be so for some time. The possible toxicity of deoxycortone, however, must be investigated before its clinical use is recommended in view of recent animal studies indicating a deleterious effect of this compound on the liver.

—*Lancet 2,* 993 (1949) —*Science 109,* 37 (1949)

Fat Absorption and Atherosclerosis:

In a recent study on the rate of fat absorption it was found that, following a fat meal, minute fat particles in the serum (chylomicrons) reached their peaks and dropped back to fasting levels at markedly different rates in young and old subjects. In a group of young subjects with average ages of 18, fat droplets in the serum reached a peak in 2½-3 hours after eating and returned to fasting levels by the end of the fifth hour. In an older group, averaging 76 years, peaks were not reached until 8-12 hours and fat droplet counts did not return to fasting levels until 24 hours later. In addition older persons exhibited a consistently and considerably higher chylomicron count. According to several current theories hyperlipemia and hyperchylomicronemia (high blood levels of fat or fat particles) are characteristic of conditions leading to abnormal hardening of the arteries (atherosclerosis).

*cf. *Borden's Review of Nutrition Research,* "Dietary Interrelationships—Vitamin C and the Metabolism of Aromatic Amino Acids," Sept. 1949.

Further, it is believed that particles the size of chylomicrons in the circulating blood can be deposited and can damage the internal layers of the arteries. Chylomicrons contain neutral fat, which eventually disappears, and cholesterol which remains and accumulates gradually, ultimately causing atherosclerosis. Whether food cholesterol or endogenous cholesterol or the irritating chylomicrons themselves are the cause of human atherosclerosis is still a matter of controversy.

Increased chylomicronemia following the eating of fat-containing food occurs at every age. However, it lasts only a short time and is only of moderate intensity in young persons. With increasing age, particularly over 50, chylomicron concentration in the blood is greater and remains so almost constantly. If the chylomicrons play a role, as believed, in atherosclerosis, the condition leading to this disease has finally been found.

A further finding of the utmost potential significance is the fact that the administration of lipase (fat-splitting enzyme) or of a fat emulsifier (the detergent, Tween 80) with a fat meal reduces the blood level of chylomicrons in older persons to the level occurring in the younger age group. No change is noted in young persons receiving lipase or Tween. Whether the use of lipase or of detergents will be of practical value in preventing atherosclerosis is a provocative question which requires considerable animal experimentation before a conclusive answer may be found.

—*Science 110,* 529 (1949)

Fat Absorption and Emulsifiers:

A possible physical-nutritional role for the emulsifying agent, Tween 80 (polyoxyethylene sorbitan monooleate, PSM) discussed above, is indicated by experiments in which it has been used to facilitate fat absorption in human subjects. Addition of PSM was found to accelerate the absorption of fat-soluble Vitamin A in normal subjects and improved faulty vitamin A absorption from 400-500 per cent in patients suffering from sprue and other gastrointestinal disorders. Loss of fat in stools due to such disorders was reduced when PSM was mixed with the food, thereby permitting weight maintenance and gain in malnourished, underweight patients.

—*Nutr. Rev.* 7, 205 (1949)

Calcium, Riboflavin, Vitamin A and Longevity:

New findings reported during 1949 confirm the results of a continuous series of animal experiments of more than 20 years duration. Increasing the vitamin A, calcium and riboflavin levels above the minimum or even "optimum" levels has been found to have marked beneficial effects upon the life

span, reproductive efficiency and vigor of experimental animals. Liberal allowances of these nutrients make possible the utilization of higher than ordinary levels of dietary protein with comparable results. Quadrupling an adequate allowance of vitamin A, for example, increased the normal life span by 10-12%; the "useful" segment, or "prime of life" is also extended; development and maturity are accelerated and old age, deferred. It is of interest to note the unique value of milk as a liberal source of all four of these nutrients. In the customary American diet, in fact, it is virtually the only reliable source of calcium and one of the few major sources of riboflavin.

—*J. Nutr.* 37, 467 (1949) —*J. Nutr.* 37, 317 (1949)

Amino Acid Metabolism In Premature Infants:

Premature infants fed cow's milk mixtures of high protein content require vitamin C in order to completely metabolize the amino acids, tyrosine and phenylalanine.* Scorbutic guinea pigs also fail to metabolize tyrosine. The defect is corrected not only by administering vitamin C, but as has been more recently found, by feeding supplements of folic acid in place of vitamin C. This overlapping function of folic acid and vitamin C has now been investigated in the human infant. Varying effects of folic acid were noted, especially depending on the method of administration (oral or intramuscular injection), but evidence for a role of folic acid in human amino acid metabolism similar to that of vitamin C—and comparable to the effects observed in scorbutic guinea pigs—was clearly indicated.

—*Science* 109, 332 (1949)

Maternal Nutrition and Infant Health:

The importance of the mother's diet in relation to well-being during and after pregnancy and to the condition of the newborn infant continues to occupy a prominent position among nutrition studies concerned directly with human subjects. New findings reported during the summer of 1949 confirm earlier reports of a large scale research program initiated in 1943 covering detailed studies of 216 mothers and their babies.** In the current study, a group of women from the earlier survey were studied. The new infants were compared both with the mother's diet and the condition of infants born in previous pregnancies to the same mothers. The close relationship between

*cf. *Borden's Review of Nutrition Research,* "Dietary Interrelationships—Vitamin C and the Metabolism of Aromatic Amino Acids," Sept. 1949.

**cf. *Borden's Review of Nutrition Research,* "Clinical Studies on Prenatal Nutrition," Dec. 1944.

good prenatal diets and the physical condition of the infant at birth is dramatically illustrated by the following findings:

1. In the 284 cases when the maternal diet was "excellent or good," 95% of the infants were in good or excellent physical condition at birth and only 5% were in either fair or poorest physical condition. In contrast, when the maternal diet was "poor to very poor" 65% of the infants were in the poorest physical condition at birth and 27% were in fair condition, while only 8% were in either good or excellent physical condition.

2. The "fair" diet group was divided into two groups, thus giving 4 maternal dietary groupings: (1) "excellent or good"; (2) "fair"; (3) "poor"; and (4) "very poor." This has helped to make clear that a "very poor" maternal diet is associated with an infant in the poorest physical condition at birth, while an "excellent or good" diet is associated with an infant in excellent or good condition at birth. The consistent shift in physical condition of the infant with each change in dietary rating in either direction is impressive.

3. The statement still remains true that all of the stillborn infants, all of the neonatal deaths but one, all of the premature infants but one (a neonatal death), all of the functionally immature infants, and most of the congenital defects were found in the group of infants born to mothers with "poor" or "very poor" prenatal diets. Since no major effort was made to change the dietary habits of these women, it is probable that in the majority of the cases the prenatal dietary rating was representative also of long-time food habits.

4. The average birth weight and birth length of the infant decreased as the maternal dietary rating became poorer. The constancy of this relationship is impressive. While a relationship exists between physical condition of infant and birth weight and length, a closer relationship is shown between maternal dietary rating for pregnancy and birth weight and length of infant.

5. Data were presented on 53 matched pairs of siblings. Improvement of the infant's condition with improvement of the maternal diet and deterioration of the infant's condition with deterioration of the maternal diet appeared in this series where each of the 53 mothers was observed through two pregnancies.

   While the changes were not sufficiently striking to be statistically significant, it is felt that this series of matched siblings is unique since it has been possible to use each mother as her own control and thus in part minimize hereditary and environmental variables which influence the condition of babies at birth. Similar studies of women through successive pregnancies may help further to clarify the relationship between prenatal diet and the condition of the infant at birth.

—*J. Nutr.* 38, 453 (1949)

Nutrition Surveys:

Practical applications of nutritional diagnostic and therapeutic procedures have been effected in large-scale population groups. Two outstanding examples are the nutrition surveys and resultant recommendations made recently in Newfoundland and in the Philippines.

Newfoundland: The nutrition survey in Newfoundland was begun in 1944 by nutritionists from Canada, the United States and England.

The study established that the people of Newfoundland subsisted on a definitely lower level of intake than those in Canada and the United States. It revealed a high incidence of clinical signs attributed to chronic deficiency of vitamin A, riboflavin, and ascorbic acid and low values for these nutrients in the blood or urine. No pellagra and little peripheral neuritis was encountered. Signs of rickets were infrequently noted and no evidence of protein deficiency was observed. Values for hemoglobin and blood phosphatase were satisfactory. Records of average height conformed fairly closely with the standards of comparison chosen. The review of this report pointed out that the unsatisfactory general health of the population of Newfoundland could not be attributed entirely to faulty dietary habits.

Re-examination of a similar sample of individuals has now been made.

Governmental and other agencies had inaugurated several measures to improve nutrition. These included an intensified educational campaign, free distribution to many schools of a dried, non-fat milk powder preparation of free cod liver oil, and of free concentrated orange juice for expectant and nursing mothers and infants under 1 year of age. In addition, after January 1945, all margarine was fortified with vitamin A, and beginning with the fiscal year 1944-45, all imported white wheat flour was enriched with niacin, riboflavin, thiamine, and iron. In 1947, this latter enrichment was extended to include bone meal in an amount sufficient to provide not less than 500 mg. of calcium per pound of flour.

During the interval between the two surveys, there was an increase in the available food supply, greatly improved economic status of the individual, increased employment, decreased isolation, considerable activity on the part of official and nonofficial agencies directed toward improving the nutrition, and, in addition, the fortification of margarine and enrichment of flour. It is apparent that these are but some of the changes which occurred on an accelerated scale during wartime and shortly thereafter. No information is provided on the importation and use of multi-vitamin preparations, of newer antibiotics, of alterations in medical-care programs, and so forth.

During the four year interval between the two surveys the vital statistics for the island indicated an improvement in health. Because of the multitude of intangibles bearing on changes of the magnitude indicated in this report, these changes cannot be interpreted in terms of nutritional status alone. Further, the method of comparison adopted by the authors makes it impossible to evaluate the rate of changes, inasmuch as they compare individual years after 1944 with averages for a five year period preceding the earlier survey.

The chemical findings demonstrate that an increased vitamin content of foodstuffs throughout the population will result in an increase in body concentration of these same nutrients. The recorded improvement in lesions of the tongue and lips associated with the known dietary alterations and demonstrated chemical changes support the thesis that there existed a considerable amount of riboflavin and possibly niacin deficiency within the population prior to the 1944 survey. Failure to observe a change in neurologic manifestations despite the more abundant thiamine intake and body stores make it apparent that the thiamine level previous to enrichment was sufficient to protect against neurologic disease and that the existing neurologic findings have their origin in some condition other than thiamine deficiency.

While one may readily disagree with the implication that certain of the physical signs recorded in this study are necessarily related to nutritional status, as well as with any effort to claim that one or two of the measures enumerated were completely responsible for all of the differences observed between the two surveys, it is apparent that these two studies demonstrate a fundamental principle: Provision of basic foods of greater nutritional value will result in an increased nutritional level of a poorly nourished population. Further, they provide evidence that additional intakes of a factor will not be followed by a betterment of a population level which is not due to a deficiency of the factor. Thus, enrichment of flour with iron did not appreciably increase hemoglobin levels and additional thiamine did not eliminate existing neurologic findings.

Bataan: A nutrition survey in Bataan in the Philippines during 1948 showed an incidence of beriberi in 12.77% of 12,400 people examined. Mortality rates were extremely high, particularly among infants and pregnant women. As a result, a food enrichment program has been begun in an attempt to improve conditions in these groups as well as among the general populace.

Preliminary trials with artificially enriched white rice (rice with added thiamine, niacin and iron) to determine its acceptability have been successful in contrast to earlier attempts to introduce brown rice, under-milled rice and similar products. Small trial groups included 1) government employees, 2) children in welfare institutions, 3) Army personnel. Appreciable weight gains

and height increases were noted in those children receiving the enriched rice as compared with control groups on ordinary white rice. Favorable effects were also noted on hemoglobin and red cell counts. A decrease in the incidence and degree of peripheral neuritis among the Armed Forces was noted. A trend toward reduction in general mortality rates is already apparent, although results of widespread distribution of enriched rice have not yet been investigated and interpreted.

—*Can. Med. Assn. J. 60,* 329 (1949) —*J. Nutr. 38,* 443 (1949)

Nutrition and Degenerative Diseases:

Recent animal studies have led to the recognition of a relatively new concept relating temporary nutrition deficiencies in infancy to the subsequent appearance of serious degenerative diseases in adulthood. A significant illustration is found in the experimental production of high blood pressure in adult rats by short periods of acute choline deficiency in infancy. The hypertension has been traced to permanent kidney damage during early life—a condition characteristic of severe choline deficiency. Several important facts have been noted: In animals maintained on a choline-deficient diet for seven to ten days, the resultant hemorrhagic kidney syndrome is so severe as to be fatal in most cases. Those few animals which are sufficiently resistant to survive, continue normally when given adequate diets and show no evidence of kidney damage or hypertension when examined at autopsy. When, however, animals are maintained on choline-depleted diets for shorter periods of about five days, hemorrhagic kidneys develop, but not to an extent causing death. Animals which develop hemorrhagic kidneys under these conditions and which are then transferred to normal diets, again depleted briefly and restored (the process repeated about four times) and permitted to remain on diets conducive to good growth, develop hypertension during adulthood. If young rats which survive the hemorrhagic kidney syndrome are kept on choline deficient diets throughout the experimental period, hypertension does not appear. If, however, the diet is made adequate by restoring choline or protein, after kidney damage occurs, malignant hypertension often results in later life. This is explained on the influence of the rate of growth. Animals on the deficient diet would grow more slowly and presumably the demands on the damaged cardiovascular system would be correspondingly lessened; also kidney metabolism would be on a lower level because of the low protein content of the diet. The investigators conclude:

> "An important outcome of this work is the proof that extensive, and often fatal, pathological changes during adult life may have their origin in a very short period of dietary abnormality in infancy. Correction of the abnormality during adult life, under certain conditions, may lead to pathological changes (hypertension in the present instance), which would otherwise not have occurred."

These studies, therefore, establish a new technique and field of nutritional

investigation. It is based on the principle of subjecting young animals to acute deficiencies of one or more essential nutrients, followed by periods of normal or superior growth rates, in an effort to reveal hitherto unsuspected effects of the initial acute deficiency.

—*Fed. Proc.* 8, 610 (1949) —*Nutr. Rev.* 7, 312 (1949)
—*Brit. Med. J.* 1, 423 (1949)

Peptides as Growth Essentials:

The nutritional adequacy of a protein is customarily determined by an analysis of its amino acid content in terms of the kinds of amino acids present, as well as the amounts of each. Recent investigations into the nutritional requirements of microorganisms have led to the recognition of a potential new basis for evaluating proteins in terms, not only of amino acid content, but of their component peptides (compounds consisting of two or more amino acids). For example, studies have been made of a microorganism which, under specific conditions, grows in the presence of a dipeptide of L-leucylglycine but not in a mixture of the two component amino acids, leucine and glycine. Nor does the microorganism grow if the dipeptide is in the form, glycl-l-leucine, a simple reversal of the two amino acids. It appears, therefore, that specific peptide linkages, rather than peptides *per se* or even their component amino acids are nutritional growth essentials under certain conditions. These findings may eventually necessitate re-evaluation of proteins not only in terms of their amino acid content but in terms of peptide make-up as well. It is not yet known whether other species have similar peptide requirements, although past studies in biochemistry have emphasized the similarity in nutritional requirements of animals and micro-organisms.

—*Science* 109, 561 (1949)

Printed in U.S.A.